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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,964	02/10/2004	Jia-Hwa Fang	PP16502.015	1609

7590

07/13/2006

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EXAMINER

FUBARA, BLESSING M

ART UNIT	PAPER NUMBER
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1618

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/775,964

Applicant(s)

FANG ET AL.

Examiner

Blessing M. Fubara

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-44 and 58-67 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-44 and 58-67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Examiner acknowledges receipt of amendment and remarks filed 05/01/06. Claims 34, 37, 39, 43 and 58 are amended. New claims 62-65 are added. Claims 34-44 and 58-65 are pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The rejection of claims 34-37, 39, 42-44 and 58-61 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using cetyl trimethyl ammonium bromide (CTAB) in the preparation of microparticles without washing the prepared microparticles, does not reasonably provide enablement for using all detergents in the preparation of microparticles without washing the prepared microparticles is withdrawn because the specification describes washing or not washing the formed microparticles. The specification does not place emphasis on the use of CTAB in the method that does not wash the prepared particles over use of other detergents.

3. However, the amendment to claim 34 raises issues described below. For example, while the 10-90% in 34(b), second line from the bottom is not held new matter because the 10-90% is present in original claim 34, the specification does not provide antecedence for that limitation in the claim. Secondly, *selecting a ratio of detergent to polymer* such that about 10-10% of the total detergent in the microparticle composition is bound to the microparticles when the microparticles are not washed or washed does not have support in the specification.

Art Unit: 1618

4. Claims 34-36, 39-44, 60-63, 66 and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The specification as originally filed does not provide support for the new limitation where specific ratio of detergent to polymer is selected to arrive at the recited ratio.

Response to Amendment

Applicant points to paragraphs [0095] to [0098] of the specification for support of the amendments and the new claims. However, the amendment to claims 34 and 39 where a selection process is involved to arrive at the recited 10-90% detergent bound to the microparticles is not found within the paragraphs cited by applicant as providing support. The 10-90% is not held as new matter since the original claims recite that range. However, applicant is respectfully requested to point to the section of the original specification that provides the support.

Objection to the specification:

The specification is objected for lacking antecedent support for selecting a specific ratio of detergent to polymer that would arrive at a 10-90% detergent bound to the microparticles.

5. The rejection of claims 34-44 and 58-61 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's argument that washing or

Art Unit: 1618

absence of washing steps in which a detergent to polymer ratio of from about 0.001 : 1 to about 0.05 : 1 is mentioned is a specific embodiment that does not establish absolute limit.

Response to Arguments

6. Applicant's arguments, filed 5/2/06, with respect to the rejections under 35 USC 112 have been fully considered and are persuasive. The rejections have been withdrawn.

Claim Rejections - 35 USC § 103

7. Claims 34-44 and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy et al. (US 6,395,253) in view of Paliard et al. (US 6,562,346). New claims 62-67 are included in the rejection.

LEVY discloses preparation of microspheres that contain DNA or RNA as the bioactive agent (column 4, lines 31, 54 and 55). LEVY prepares a double emulsion of water-in-oil-in-water emulsion by using a condensing agent in one phase and the method comprises the steps of: "(a) dissolving at least one polymer in a water-immiscible organic solvent to yield an organic phase; (b) dissolving a polyanionic bioactive agent in aqueous solution to yield a first aqueous phase; (c) emulsifying the organic and first aqueous phases to yield a first milky emulsion; (d) dissolving a condensing agent in aqueous solution to yield a second aqueous phase; (e) emulsifying the first milky emulsion and the second aqueous phase to yield a second milky emulsion; and (f) removing the organic solvent from the second milky emulsion to yield microspheres containing condensed polyanionic bioactive agent. The removal of the organic solvent in the final step is preferably by means of evaporation." DNA and RNA are

Art Unit: 1618

macromolecules and are polynucleotides. The concept of microspheres meets the microparticle limitation. Regarding the recitation that the microparticles are not subjected to washing step, it is noted that while the examples in Levy disclose a wash step, the basic preparation disclosed by Levy in section 4.2 does not state a wash step but rather that the microspheres are collected by ultracentrifugation and the alternative protocol disclosed in 4.6. Levy uses 0.1% detergent (SDS in this case). There is no demonstration in applicants' specification that not subjecting the microparticles to a washing step provides unusual/unexpected results to the microparticles. The claims do not recite amount of detergent added to make the microparticle in the emulsion.

Regarding claim 36, which is directed to the process of cross-flow filtration, it is noted that in the cross-flow filtration process of the examined application, four liters of deionized water is used to remove the detergents and this appears to be equivalent to washing. There is also no demonstration that the cross-filtration step performed after removing the organic solvent provides unusual results; Levy discloses filtration as one of the steps.

Regarding the ratio of lactide to glycolide, it is noted that there is no demonstration by applicants that the recited ratio provides unusual/expected results. The silence of Levy on the ratio of lactide to glycolide is an indication that the lactide/glycolide can be used in any desired ratio that would be effective as a condensing agent for the DNA or RNA.

Levy uses SDS detergent. Levy does not disclose the use of cetyl trimethyl ammonium bromide (CTAB) detergent. But Paliard discloses an emulsion that comprises PLG polymer and CTAB (Example 5). Thus Paliard is relied upon for a teaching that the specific CTAB detergent can be used with PLG in an emulsion. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the double emulsion of Levy where

Art Unit: 1618

the emulsion comprises a detergent and PLG and a solvent. One having ordinary skill in the art would have been motivated to use the CTAB of Paliard in place of SDS with the expectation that the CTAB will interact with the composition to aid the DNA containing microsphere to disrupt to release the DNA.

Response to Arguments

8. Applicant's arguments filed 5/1/06 have been fully considered but they are not persuasive.

Regarding applicant's argument that Levy does not indicate that the presence of substantial amount of detergent with the microsphere or particles, it is noted that Levy does not disclose that the microspheres are devoid of detergent. Furthermore, regarding the argument that in Levy, the detergent does not form a complex with the macromolecules, it is noted that the claims do not recite complex formation between the detergent and the polymer. Regarding applicant's statement about 10-90% on page 11, indented paragraph, it is noted that applicant argues against examiner's response without providing an argument. Levy's washing and centrifugation steps are all the washing steps because centrifugation is a process of separating solvent from particles and centrifugation can be considered filtration in which the solvent is separated from the particles.

9. Claims 34, 35, 36, 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hagan et al. (US 6,086,901).

O'Hagan discloses the process of preparing an emulsion that comprises poly(lactide-glycolide), solvent and detergent (Example 1); O'Hagan discloses that the size of the droplets (particle, microsphere) depends on the ratio of the detergent to oil (column 12, lines 38-47) and

Art Unit: 1618

also that water-in-oil-water (w/o/w) type emulsion can be formed of the microparticle (column 10, lines 9-20). The process of claim 36 reads on washing because in the cross-flow filtration process, 4 liters of deionized water are used and the removal of the water appears to approximate the process of filtration/washing. While O'Hagan discloses a washing step, there is no demonstration in applicants' specification that not subjecting the microparticles to a washing step provides unusual/unexpected results to the microparticles. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare microparticle according to O'Hagan. One having ordinary skill in the art would have been motivated to do so with the expectation of producing biodegradable microparticles for administration to vertebrates to effect immunization and in the absence of unexpected results, the exclusion of the washing step does not patentably distinguish the invention, which uses 4 liters of water in a cross-flow filtration, over a process that washes the microparticles.

Response to Arguments

10. Applicant's arguments filed 5/1/06 have been fully considered but they are not persuasive.

Regarding applicant's argument that O'Hagan does not suggest that the process of producing the particles should ensure that the particles contain substantial amount of unbound detergent, it is noted that O'Hagan does not teach against producing particles that have substantial amount of unbound detergent.

11. Suggestion:

The full name cetyl trimethyl ammonium bromide may initially used and the abbreviation CTAB expressed in parenthesis for subsequent use.

Art Unit: 1618

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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